Craniofacial manifestations of Down syndrome: A review of literature

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ABSTRACT

Down syndrome (DS), which is also known as DS; trisomy G; and mongolism, is a congenital autosomal (non-sex chromosomes) anomaly characterized by a deficiency in general and mental development, affecting one in six hundred to one in two thousand live births in different populations. Individuals with Down syndrome have various characteristic physical and systemic manifestations with the craniofacial manifestations being the most distinctive.

Key words: Down syndrome, craniofacial manifestation, cephalometric, airway.

INTRODUCTION

Down syndrome is a genetic disorder that results from a chromosomal abnormality due to trisomy of all, or a large part of chromosome (Hamerton, 1971). In the past, DS was known as mongolism. In the report of Howard (1979), the World Health Organization (WHO) officially dropped references to the name after a request by the Mongolism delegate. Presently, this condition is known as Down syndrome, trisomy (Desai, 1997), or trisomy G (Desai, 1997).

INCIDENCE AND ETIOLOGY

Down syndrome is the most recognized congenital autosomal anomaly associated with delayed physical and mental development (Jensen et al., 1973). About 5 to 10% of all mentally retarded children are affected by DS (Spitzer et al., 1961; Jensen et al., 1973). Suri et al. (2010) reported no racial, social, economic, or gender predilection for Down syndrome incidence. It occurs in all ethnic groups and geographical regions. However, according to Horbelt (2007), the incidence of DS has been found to be variable when studied in different populations.

A literature review performed by Carothers et al. (1999) showed variation between population groups such as increase in rates among United States residents of Mexican or Central American origin, low rate among Afro-Americans, and a higher rate in Israeli Jews of non-European origin. The birth prevalence of DS is generally stated to be 1/650 live births, but it is known to vary in different populations from 1/600 to 1/2000 live births. Fifteen percent of patients institutionalized for mental retardation have DS (Lilienfeld and Benesch, 1969; Hamerton, 1971; Smith et al., 1976). It has been estimated that 65 to 80% of DS conceptions results in spontaneous abortions (Smith et al., 1976). A study by Niazi et al. (1995) was carried out in Riyadh (Saudi Arabia) to determine the incidence and distribution of DS births, during a 9-year period from July, 1982 to June, 1991. DS was ascertained in 42 (23 females and 19 males) of 23,261 consecutive babies born alive to Saudi women, giving an incidence of 1 in 554 live births (1.8 per 1,000).

The exact cause of this syndrome is currently unknown; however, maternal age has been associated with the increased incidence. DS occurs in 1 in every 1550 live births in women younger than 20 years, in contrast to 1 in 25 live births in women older than 45 years. The reason for the increased susceptibility is not yet fully understood (Desai, 1997). Diagnosis of DS can be confirmed cytogenetically. The extra 21st chromosome is detected using a technique called Karyotype. A karyotype is a visual display of the chromosomes grouped by size, number and shape (Langman and Sadler, 1955).

The most common form of DS is a non-disjunction error which occurs during cell division. All individuals with DS have an extra chromosome (Hamerton, 1971) or critical
portion of this chromosome present in all or some of their cells. This additional genetic material alters the course of development giving rise to the characteristics associated with the syndrome (Gardner and Sutherland, 2004; Langman and Sadler, 1955).

**PHYSICAL AND SYSTEMIC MANIFESTATIONS**

**General manifestations**

Patients with DS present numerous characteristic clinical findings and systemic manifestations (Gorlin et al., 2001). Limb findings include short stature, muscle hypotonia, single palmar crease, hyper flexibility of the joints, curvature of the fifth finger, and excessive space between the first and second toe. These physical findings are associated with generalized growth retardation and varying degrees of mental retardation (Gorlin et al., 2001; Langman and Sadler, 1955; Smith and Berg, 1976). They are also at an increased risk for a number of medical conditions (Desai, 1997; Horbelt, 2007; Smith et al., 1976).

The most significant condition is congenital heart defects, which occurs in approximately 40% of subjects. They are also susceptible to several infections such as dermal, mucosal, gastrointestinal and respiratory infections (Desai, 1997; Horbelt, 2007). A greater risk of leukemia which affects approximately 1 in 200 can be found in children with this syndrome (Desai, 1997). Endocrinical problems especially hyperthyroidism and hypothyroidism are reported as well in several cases with DS (Smith et al., 1976; Dinani and Carpenter, 1990; Mhçi et al., 2010).

Motor function is usually delayed in younger patients and may lead to restricted co-ordination; however, co-ordination was found to improve with age (Desai, 1997). Conductive and sensori-neural hearings loss occurs in up to 70% of patients and sometimes may not develop until early adulthood (Smith et al., 1976). Dementia which can start at an early age affects about 30% (Regezi and Sciubba, 1999). About 22% of individuals also manifest psychiatric disorders (Horbelt, 2007). Behaviour problems include non-compliance, aggression and self-injury, but most DS patients often respond to behaviour management techniques (Horbelt, 2007; Smith et al., 1976). Majority of individuals with DS have some degree of intellectual disability. They are considered to function in the mild range of retardation with an intelligence quotient (IQ) of 20 to 50 (Regezi and Sciubba, 1999; Horbelt, 2007). The overall prognosis for individuals with DS has improved remarkably in recent years owing to better control of infections, advanced medical care and greater acceptance from the society (Horbelt, 2007; Kumar et al., 1999).

Over the last 80 years, the life expectancy of a person with DS has increased significantly. In 1929, the average lifespan for a child with DS was only nine years. By 1980, this number had increased to approximately 30 years of age. In 2006, it was reported that a person with this condition could expect to live up to 56 years (Horbelt, 2007).

**Airway disorders**

An array of congenital airway anomalies occurs among Down syndrome patients. The airway of DS subjects has been described as tenuous, especially during operative procedures (De Jong et al., 1997). One of the main features of DS is Midface hypoplasia and hence, the naso-pharyngeal and oro-pharyngeal regions for patients expected to be narrower and of smaller volume; this has been reported from a direct assessment of the naso-pharynx in Down syndrome subjects that is significantly decreased (Strome, 1981).

Clinical studies showed that obstructive sleep apnea, which is the most common type of sleep disorders caused by obstruction of the upper airway is present in approximately 30 to 55% of children with DS (Taylor and Lachman, 1996; Cohen, 2005). The predisposing factors for this condition in children include facial (midfacial hypoplasia and mandibular hypoplasia) and other physical features (Glossoptosis, an abnormally small upper airway, superficially positioned tonsils, relative tonsillar and adenoidal encroachment and hypotonia of upper airway) (Marcus et al., 1991; Roche et al., 2003). Adults with DS as well, are at increased risk for obstructive sleep apnea, as these predisposing factors observed in children continue into adulthood.

The rate of hypothyroidism increase in adults with DS has also been found to be associated with obstructive sleep apnea. The few studies that have examined the rate of obstructive sleep apnea among adults with DS report that up to 94% of adults suffer from this disorder (Trois et al., 2009).

**Disharmonies of occlusion**

It has been reported that individuals with DS display malocclusion and mal-alignment of teeth to a greater extent than normal people (Desai, 1997; Horbelt, 2007). These include anterior open bites, anterior and posterior cross bites, crowded teeth, widely spaced teeth, dental protrusions and a high prevalence of Class III malocclusion (Gorlin et al., 2001; Ferrario et al., 2005).

Cohen and Winer (1965), in their clinical study of 123 DS (3 to 30 years old) observed open bites in 4.8% of the 56 DS patients they examined. Kisling (1966) reported a higher percentage of anterior open bites found in about 54% of DS patients. A similar finding was established by Jensen et al. (1973) in his study of 129 Caucasian subjects with DS (69 males and 60 females) where anterior open bites was observed in 55.8% of their study sample. In another study,
Vigild (1985) clinically examined 37 DS cases and recorded that 38% of them had anterior open bites. A lower prevalence was reported by Oliveira et al. (2008), who clinically studied 112 DS patients (3 to 18 years old) and found anterior open bites in only 21%. A considerable number of studies have documented the prevalence of anterior and posterior cross bites in DS subjects.

Jensen et al. (1973) in their study found 15.5% of the cases had anterior and posterior cross bites. Another study by Oliveira et al. (2008) observed that 33% also have this abnormality. When posterior cross bite was studied separately, Kisling (1966) found posterior cross bites in 97% of 40 DS cases and Jensen et al. (1973) reported a prevalence of 56 and 55%, respectively. Ondarza et al. (1995) in their study based on clinical examination showed a higher frequency of mal-alignment and crowding in both the deciduous and permanent dentition of the DS group in comparison to a non-syndromic group.

Similar results were reported by Kisling (1966), who found Class III malocclusion, in 65% of the Down subjects he examined (Desai, 1997). Moreover Jensen et al. (1973) and Vigild (1985) also reported similar findings of Class III with a range of 50 to 58.9%, respectively. A similar study by Cohen and Winer (1965) found that Class III malocclusion was present to a slightly less degree than the previous mentioned studies, which was 46.4% of the 56 DS patients with an age range from 13 to 30 years. Cohen et al. (1970) reported even a lower prevalence of Class III malocclusion, which was in only 22% of the Down cases they studied. Until now, the majority of studies have demonstrated that Class III is the most common malocclusion found among DS subjects.

Contrary to the aforementioned, Cohen et al. (1970) concluded from their findings that Class I malocclusion was actually more prevalent in these subjects. Cohen et al. (1970) based on dental casts of 50 DS subjects found that 46% of DS patients presented with Class I malocclusion compared to 22% with Class III. Similarly, Cohen et al. (1970) based on clinical examination, concluded that 51% of the DS subjects in his study had a Class I malocclusion compared to 47% of patients with Class III. Class II has also been reported previously, but to a much lesser frequency, ranging from 0 to 32% in Down subjects (Cohen et al., 1970; Cohen and Winer, 1965).

Craniofacial clinical manifestations

The craniofacial manifestations in DS subjects are among the most characteristic findings which produce the typical facial appearance of this syndrome (Gorlin et al., 2001). These include brachycephaly, hypoplasia of the midfacial region, depressed nasal bridge, slanting eyes with epicanthic folds, hypotelorism, strabismus and small ears with flat or absent helix. Some of the facial findings observed are not abnormal by themselves; however, the total constellation of manifestations is distinctive (Desai, 1997; Gorlin et al., 2001).

In DS subjects, the skull has been frequently reported to be brachycephalic with a flat occiput, associated with a decreased length and flattening of the cranial base (Horbelt, 2007). Levinson et al. (1955) studied the variability of clinical features in 50 DS subjects up to 17 years of age. In their observations, they noticed that 82% of the patients presented with brachycephaly had a flat occipit. Al-Shawaf and Al-Faleh (2011) compared thirty Saudi DS group to thirty non-syndromic group (age range: 12 to 24 years) based on clinical examination and found that 53% of DS subjects had brachycephaly. Studies have shown that although variable shapes of the nose are present in DS cases, certain features are consistently observed. Among these is flatness of the nasal bridge associated with underdeveloped or absence of the nasal bones (Regezi and Sciubba, 1999; Ferrario et al., 2005).

In a clinical study performed by Levinson et al. (1955) on 50 children with DS, a depressed nasal bridge was observed in 82% of the cases, whereas Cohen and Winer (1965) reported this in 77.6% of their cases. The highest prevalence was found in the study conducted by Al-Shawaf and Al-Faleh (2011) which was found to be present in 93.3% of their subjects.

Another commonly observed feature in DS cases is slanting of the eyes (where the outer corner of the eye is slanted in an upward direction) and epicanthic folds (extra vertical folds of skin of the upper eyelid which cover the medial canthus of the eye). Levinson et al. (1955) reported slanting of the eyes and epicanthic folds in 88 and 50% of DS patients, respectively. Moreover, Cohen and Winer (1965) reported both at the same time in 78% of the DS subjects. A higher prevalence of these findings was found in the study of Al-Shawaf and Al-Faleh (2011) where 93.3 and 66.7% of their Down subjects were affected by slanting eyes and epicanthic folds, respectively. Regarding oro-facial manifestations, studies have shown that open mouth is a common trait found in DS subjects (Oster, 1953; Levinson et al., 1955; Smith and Berg, 1976). Oster (1953) reported this clinical finding in 67% of the cases. Similarly, Levinson et al. (1955) reported this manifestation in 62% of the patients whereas, this condition was not a common finding in a more recent study conducted by Cohen et al. (1970), in which this feature was present in only 10% of the patients.

Craniofacial radiographic features

Various radiographic manifestations of the craniofacial region have been reported in DS subjects. These include brachycephaly, microcephaly, thin calvarium with wide sutures and delay in closure, hypoplasia of the facial bones, short hard palate, absent or poorly developed air sinuses, and small rudimentary nasal bones (Gorlin et al., 2001;
Cliff (1922) noted that a thin cranial bone was present in radiographs of subjects with DS. Spitzer et al. (1961) observed a thin calvarium in 93.1% of the Down cases using postero-anterior and lateral radiographs. Frostad et al. (1971) reported thinning of the cranial bones based on a subjective evaluation of postero-anterior radiographs of different ages of Down patients. This thinning was evident in the frontal and parietal bones, with an almost total absence of dipole formation.

Delayed closure of sutures is also considered as one of the radiographic manifestations present in Down subjects by several investigators (Roche et al., 2003; Quintanilla et al., 2002; Spitzer, 1955). Spitzer et al. (1961) studied the radiological changes in 28 DS subjects with an age range of 7 to 29 years old, using posteroanterior and lateral radiographs, and compared it with 27 mentally disabled subjects without DS. In the DS group, delayed closure of sutures was found in 21.4%, in comparison to 5% in the mentally disabled subjects.

Spitzer and Quilliam (1958) in a comparative study observed the congenital anomalies in the skull in two groups of mental defectives (mental disabilities) using posteroanterior radiographs (one group with DS and the other group without DS). Among the DS group, metopic sutures (persistent frontal sutures) were found in 75%. In addition, 15% of DS cases were found to have metopic sutures with another persistent cranial suture. However, these percentages in the other group (non-Down) were 20 and 5%, respectively. Absent or poorly developed air sinuses is another feature reported by several researchers. Absent and hypoplastic frontal air sinuses were observed in 89.3 and 3.6%, respectively by Spitzer and Robinson (1955). In another study, Spitzer and Quilliam (1958) found that frontal air sinuses were missing in all of their Down cases, while Spitzer et al. (1961) observed frontal air sinuses agensis in 82.7% of the 29 patients examined. Similarly, Frostad et al. (1971) using postero-anterior radiographs, reported bilateral frontal air sinuses agensis in 85% of the patients aged 4 to above 19 years, and unilateral agensis in 5.1% of the cases. Absent and/or hypoplastic maxillary sinuses were found in 40% of Down subjects in a study conducted by Spitzer and Quilliam (1958), but on the other hand, were not a common finding in a study carried out by Spitzer and Robinson (1955) where it was reported to be 3.6% as totally absent and 10.7% as hypoplastic.

Frostad et al. (1971) investigated DS cases using cephalometric radiography to determine if these individuals have a distinct craniofacial phenotype and to observe these changes with growth. The sample consisted of 121 individuals (proven by cytogenetic analysis as having an extra chromosome 21) and 120 normal or control individuals. The individuals of both groups varied in age from four to fifty-three years and were divided into six age ranges. Their results concluded that the overall size of the craniofacial complex was smaller in the DS group at 4 years of age and remained smaller into adulthood. A prominent forehead was noted in the DS group, as well as other abnormalities in the frontal region. Growth changes occurred, however, to make the forehead more sloping and the maxilla less retrusive in appearance with age. Marked differences from normal were also noted in the orbital region. The DS group, therefore, had different phenotype by the age of four years; individuals remained different throughout growth, but did show growth at the same rate and in the same direction as in the normal group. Subtle growth changes in the Down individual could account for the adults not obviously showing the characteristic clinical signs often found at a younger age.

Fink et al. (1975) used lateral cephalograms of seventy-seven males with DS and compared them with matching-age normal subjects. They concluded that the sagittal area of the endocranium, the area of the midfacial region, and the area of the mandible in subjects with DS, is significantly smaller than normal.

Fischer-Brandies et al. (1986) reported that both the maxilla and mandible in DS patients exhibit hypoplasia at birth, but stated that the growth pattern is in part comparable to that of healthy individuals. In a subsequent study, Fischer-Brandies (1986) analyzed the craniofacial development in (1896) patients with DS with an age range from 0 to 14 years. Their findings revealed that the maxilla was under-developed when compared to normal subjects.

In a subsequent study, Quintanilla et al. (2002) studied 39 patients with DS (24 boys and 15 girls) with age range (7 to 18 years) and found that the analysis of craniofacial parameters indicated average values within the clinical norm for facial and maxillary depths, facial axis and mandibular plane angle, showing a pattern of normal vertical growth in the lower facial third. They also reported that patients with DS who are in a period of growth demonstrate reduction of the anterior skull base. Protrusion and proclination of lower incisors, which is related to a tendency of anterior cross-bite and, to a lesser extent, diminished overbite were also present.

Recently, Suri et al. (2010) performed a study on 25 patients (mean age: 15.1 years) with DS and compared them to normal subjects. They found that large differences were measured in the size and spatial relationships of the craniofacial structures in the DS group. The greatest differences included a larger cranial base angle; reduced elevation of sella from Frankfurt horizontal plane; reduced anterior and posterior cranial base lengths and facial heights; smaller maxilla with reduced anterior basal and apical dimensions; and smaller mandibular ramus and body. Anterior open bite was frequently noted with a forward rotation pattern of both maxillary and mandibular planes. Maxillary incisors were severely proclined and infra-erupted (Suri et al., 2010).

A more recent study by Alio et al. (2011) assessed the
maxillary growth in a sample of patients diagnosed with DS. The sample of their study comprised 47 subjects (25 boys and 22 girls) with DS and 38 subjects without. All patients had at least two radiographs that showed the cranial base.

They found that the maxilla in DS subjects showed hypoplasia in both the vertical and the sagittal planes with a mean deficit of almost 10 mm in the latter. Upon closer examination of lateral cephalometric radiographs, other structural differences were noted. Russell (1999) analyzed the shape of sellaturcica in a group of patients with Down syndrome. Profile radiographs from 78 patients (mean age ≈ 10 years) were analyzed. A tracing was made of each sellaturcica, and the shape compared with that of a normal sella. Their findings detected an abnormal sellaturcica shape in 18 of the DS subjects. Other anomalies detected were those associated with the cervical neck. It was observed that Atlanto-Axial instability was found in 12 to 20% of DS individuals. This condition is mostly asymptomatic and diagnosed on lateral radiographs by an enlarged anterior atlantoodontoid distance (Ali et al., 2006).

Ali et al. (2006) evaluated forty-four Kuwaiti subjects with DS with an age of ≥15 years, both clinically and radiographically. Lateral radiographs were taken in the neutral and flexion positions. Asymptomatic Atlanto-Axial instability was diagnosed in eight subjects (18%), while congenital anomalies of C₁ to C₂ were found in five (12%). Three of the patients with Atlanto-Axial instability had odontoid anomalies contributing to the condition. Cervical spondylosis was also noted in 16 (36%) subjects, a comorbidity that puts the spinal cord at increased risk. Vastardis and Evans (50) reported that cephaleometric radiographs can be used by clinicians as a potential resource for screening of pathologic abnormalities of the cervical spine and potentially averting some pathologic complications.

REFERENCES
Oster J (1953). Mongolism: A clinico-geological investigation comprising 5826 mongols living on Seeland and neighboring islands in Denmark, Copenhagen, Danish Science Press, Ltd.
Smith G, Maurice B, Penrose L (1976). Down’s Anomaly 2nd ed., Edinburgh:
Churchill Livingstone.

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